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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,324	10/17/2005	Roger R. C. New	117-564	9059

23117 7590 10/23/2007

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EXAMINER	
AUDET, MAURY A	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
10/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,324	NEW, ROGER R. C.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-32,34-37,39-44,46-51,53-55,57 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-32, 34-37,39-44, 46-51,53-55, 57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/07, 04/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The present application has been transferred from former Examiner Khana to the present Examiner.

[It was previously noted that applicant's arguments pertaining to the rebuttal of the general lack of unity inventive finding made by the Examiner is found persuasive. Based on the Applicant's arguments the Examiner has rejoined the method claims.]

Applicant's amendment, response and filing of a Terminal Disclaimer over copending 10/553,169 are acknowledged. Amended claims 30-32, 34-37, 39-44, 46-51, 53-55, 57 and 58 are pending and examined on the merits. Applicant's have stated that the amendments specifically incorporate three limitations to the present compositions: 1) that the active principle is a peptide; 2) pH range; and 3) enteric coated (e.g. for oral administration).

Applicant has provided no arguments of record other than to state the present amendments should put the claims in condition for allowance per the interview discussion on 5/17/07. It is noted that an Interview Summary (as asserted by Applicant in the present response) was not found to have been placed in the file by the former Examiner (regarding the Interview of 5/17/07). So, the present action is being sent without sufficient information therein to factor any such substantive matters herein.

As to Applicant's amendments, they have been considered but are not persuasive over the 112 1st Written Description and 35 USC 103 rejections of record:

112 1st Written Description: As to the issue of "possession" at the time of the invention and as related to the previous rejections discussion of peptides within the description, the latter remains

uncertain as any and all peptides, or derivatives and analogues thereof, for which Applicant would have had "possession" of at the time of the invention.

[As to Enablement Rejection: Successfully Traversed by Cancellation of Claim 56. As to the issue of "undue experimentation" by one of skill in the art, this rejection has been dropped based on the cancellation of claim 56 and subject matter thereto, namely, treating any and all diseases.]

35 USC 103:

Regarding the issue of whether the present invention remains an unobvious contribution over the art, this Examiner is not yet convinced by the present amendments. Namely, that the prior art of record, combined with the ordinary skill of one in the art (a PhD chemist working in the field of oral peptide pharmaceuticals preparations), would not have motivated the skilled artisan to arrive at an enteric coated composition comprising ANY peptide or ANY derivative/analogue of certain known peptide genuses (inherently permeable at neutral pH of 7) AND a known aromatic alcohol (which inherently works as an absorption enhancer in the product). The functional effect of the alcohol in the product bears no patentable weight in regards to the mixing of peptides and alcohols in products. As to the method of enhancing absorption of such a product, alcohols are no absorption enhancers, and the selection of known aromatic alcohol to carry out the same would have been merely a matter of routine optimization by the skilled artisan, if not taught/suggested by the prior art of record. Applicant has provided no substantive data or otherwise on the record to substantiate that the claimed alcohol has provided a clearly unexpected result over any other known alcohol as an absorption enhancer or over the teachings/suggestions within the prior art of record.

The rejections have been repeated below, and clarity added as necessary, for continuity of record, as applied to the amended claims.

Claim Rejections - 35 USC § 112 1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

I. Written Description

Claims 30-32, 34-37, 39-44, 46-51, 53-55, 57 and 58 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons set forth above. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the claims recite a broad genus of compounds comprising an "active macromolecular principle" further comprising polypeptides, polynucleotides and polysaccharides taken in combination with an aromatic alcohol and a solubilization aid. While

structural limitations or specific functional limitations of the "genus" represented by "polypeptides" in combination with aromatic alcohols and solubilization aids are provided, no structural limitations are provided of the genus represented by polynucleotides or polysaccharides in combination with aromatic alcohols and solubilization aids. Further it is not clear what activity is required of the pharmaceutical composition comprising the "active macromolecular principle". What is the disease that is being treated by the administration of the "active macromolecular principle"? How do these activities/diseases correlate with the structure of the "active macromolecular principle" that is administered?

The specification discloses a long list of "polypeptides", and "polynucleotides" whose structures appear to vary greatly. While some of the substances such as calcitonin, and insulin are quite specific, others such as "proteins which are able to cause replication", are a broad genus that is unclear. Among the polynucleotides, while nucleotides that encode for a cytokine such as IL-1 is quite specific, others such as polynucleotides that encode an extracellular protein, are a broad genus that is unclear.

As discussed above, there does not appear to be any core structure present in the "active macromolecular principle", or the disclosure of a specific structure that will give rise to an intended activity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Therefore, the inventor, at the time the application was filed was not in possession of the broad genus comprising the "active macromolecular principle" taken in combination with an aromatic alcohol and solubilization aid needed to practice the claimed

invention. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30-32, 34-37, 39-44, 46-51, 53-55, 57 and 58 remain rejected under 35 U.S.C. 103(a) as being unpatentable over New (WO 02/28436) in view of New (USPN 5,853,748), Chakravorty (WO 02/022158) and Ivanovic (Chromatographia (1995) 40:652-656), for the reasons set forth above.

The instant claims are drawn to pharmaceutical compositions comprising an active molecular principle, an aromatic alcohol, a solubilization aid, and methods of enhancing the absorption of an active macromolecular principle comprising administering to a patient the above-mentioned pharmaceutical composition.

With respect to the composition claims 30-45, 57-58, New ('28436) disclose compositions for oral administration comprising a macromolecule, such as insulin (Example 1) or heparin, further comprising an aromatic alcohol, such as benzyl alcohol (Example 1), wherein the comprises comprises up to 75% by weight of the aromatic alcohol (page 7, lines 25-30). New ('28436) also discloses solubilization aids such as amphiphiles (page 8, lines 15-20) to improve the solubility of the macromolecule in the aromatic alcohol. Further New ('28436) disclose that the compositions of active principal, alcohol and amphiphile can be co-dissolved in the aqueous phase or the water removed by lyophilization (page 10, lines 1-5). In addition New ('28436) disclose enteric capsule of the composition of the invention to withstand the conditions of the stomach, wherein the enteric becomes permeable at a pH from 5.5 to 7 (page 7, lines 10-15).

With respect to the method claims 46-56, New ('28436) discloses methods to treat a patient with a disease that comprises the administration of the above-mentioned composition, wherein the composition enhances the absorption of the active principal across the intestinal walls (claims 26-28).

New ('28436) differs from the instant claims by not explicitly reciting that the aromatic alcohol is selected from butylated hydroxy toluene (BHT), butylated hydroxy anisole (BHA), and propyl gallate.

With respect to claims 30-58, Chakravorty discloses that it is known in the art to formulate immunosuppressive drugs with BHT, propyl gallate or benzyl alcohol wherein such agents are antioxidants, and preservatives respectively (page 6, lines 25-30).

With respect to claims 30-58, New ('748) disclose that it is known in the art that compositions that buffer the pH of the digestive tract enhance the absorption of proteinaceous materials (abstract, claim 1). New ('748) disclose the presence of sodium bicarbonate in compositions alongside bile salts and proteinaceous materials, for methods to enhance permeation in the gut (claim 18).

With respect to claims 30-58, Ivanovic disclose that it is known in the art that preservatives and antioxidants such as BHT exhibit pKa's in the range 7.5 to 9. Further, Ivanovic disclose that the ratio of the amounts of ionized antioxidant to unionized antioxidant determines the final pH of the solution.

In view of the above teachings, it would have been obvious to one of ordinary skill in the art to substitute the benzyl alcohol in the formulation of New ('28436) with BHT or BHA, for the known and expected result of proving a means recognized in the art for adjusting the intestinal milieu to enhance the absorption of proteinaceous materials.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MA, 10/15/07